K091025

BIOMÉRIEUX

510(k) SUMMARY

MAR - 2 2010

A. 510(k) Submission Information:

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Date of Preparation:	April 8, 2009

B. Device Name:

Formal/Trade Name:	chromID™ VRE Agar
Classification Name:	Culture Media, Antimicrobial Susceptibility Test, Excluding Mueller Hinton Agar. 21 CFR 866.1700
Common Name:	Culture media

C. Predicate Device: Remel Bile Esculin Azide Agar w/6µg/ml Vancomycin, K972359

D. 510(k) Summary:

Intended Use:

chromID™ VRE agar is a selective and differential chromogenic medium containing 8 µg/mL of vancomycin, for the qualitative detection of *Enterococcus faecium* and *E. faecalis* showing acquired vancomycin resistance (VRE) in stool specimens. chromID™ VRE agar can be used as an aid to identify, prevent and control VRE colonization in healthcare settings. chromID™ VRE agar is not intended to diagnose VRE infection nor to guide or monitor treatment for infections. Subculture to non-selective media (e.g. trypticase soy agar with 5% sheep blood) is needed for further identification, susceptibility testing and epidemiological typing.

Device Description:

chromID™ VRE agar is a selective chromogenic medium for the detection of *E. faecium* and *E. faecalis* showing acquired vancomycin resistance (VRE), in at risk patients[1]. The detection of this resistance is particularly important for the prevention and epidemiological surveillance of these infections and also to prevent the emergence of vancomycin-resistant *Staphylococcus aureus* (VRSA), by transmission of the *vanA* gene [2,3]. In this context, the use of chromID™ VRE agar contributes to the active surveillance for VRE. chromID™ VRE agar is a selective and differential chromogenic medium for the qualitative detection of *E. faecium* and *E. faecalis* showing acquired vancomycin resistance (VRE), from stool specimens.

chromID™ VRE agar consists of a rich nutritive base including a variety of peptones. It also contains two chromogenic substrates and a mixture of antibiotics including vancomycin (8 µg/mL) which enable the specific and selective growth of VRE. After 24-48 hours incubation vancomycin-resistant *E. faecium* colonies are a violet color for β-galactosidase-producing strains. Vancomycin-resistant *E. faecalis* colonies are a blue-to-green color for α-glucosidase-producing strains. The selective components in the medium inhibit enterococcal strains that do not express acquired vancomycin resistance, enterococcal strains that express natural intrinsic vancomycin resistance (vanC phenotype: *E. gallinarum* and *E. casseliflavus*), as well as most Gram-negative and Gram-positive bacteria.

Substantial Equivalence

chromID™ VRE agar is substantially equivalent to Remel Bile Esculin Azide Agar w/ 6 µg/ml Vancomycin (K972359) .

Device Comparison Table

	Device **chromID™ VRE Agar**	**Predicate** **Remel Bile Esculin Azide Agar w/ 6 µg/ml Vancomycin**
Similarities		
Intended Use	chromID™ VRE agar is a selective and differential chromogenic medium containing 8 µg/mL of vancomycin, for the qualitative detection of *Enterococcus faecium* and *E. faecalis* showing acquired vancomycin resistance (VRE) in stool specimens. chromID™ VRE agar can be used as an aid to identify, prevent and control VRE colonization in healthcare settings. chromID™ VRE agar is not intended to diagnose VRE infection nor to guide or monitor treatment for infections. Subculture to non-selective media (e.g. trypticase soy agar with 5% sheep blood) is needed for further identification, susceptibility testing and epidemiological typing.	REMEL Bile Esculin Azide Agar w/ 6 µg/ml Vancomycin is a solid medium recommended for use in qualitative procedures as a screening method for primary isolation and presumptive identification of vancomycin resistant enterococci (VRE) from surveillance cultures.
Test method	Manual	Manual
Inoculum	Direct Specimen	Direct Specimen
Specimen	Stool samples	Urine, stool
Differences		
Detection method	Two chromogenic substrates provide for the direct detection of *E. faecium* and *E. faecalis* through characteristic colony color. - *E. faecium* : violet color for β-galactosidase-producing strains, - *E. faecalis* : blue-to-green color for α-glucosidase-producing strains.	Organisms positive for esculin hydrolysis hydrolyze the glycoside esculin to esculetin and dextrose. The esculetin reacts with the ferric citrate to form a dark brown or black complex, esculetin, which reacts with the ferric ammonium citrate to produce a black-brown complex in the medium.
Incubation Conditions	35-37°C in aerobic conditions, in the dark.	33-37°C in aerobic conditions or in 5-10% CO_2

Performance

Performance of chromID™ VRE was evaluated at four geographically diverse laboratories. Stool specimens were inoculated on chromID™ VRE agar and bile esculin azide agar with 6 µg/ml vancomycin (BEAV). Both plates were observed for growth at 24 and 48 hours. Colonies with violet or blue-to-green pigment on chromID™ VRE agar and colonies on BEAV with brown to black pigment diffusing into the medium were identified with the following methods: Gram stain, catalase, VITEK® 2 GP and 16S-500 sequencing. Vancomycin resistance was confirmed by agar dilution.

A total of 1299 stool samples were evaluated with chromID™ VRE agar. Compared to the conventional reference methods described above chromID™ VRE identified 97.1% of the VRE positive samples and 99.7% of the VRE negative samples after 24 hours incubation. chromID™ VRE identified 96.9% of the VRE positive samples and 99.7% of the VRE negative samples after 48 hours incubation.

Performance vs. Conventional Methods

Table 1

	Positive % Agreement	**Negative % Agreement**
chromID™ VRE agar @24h incubation	97.1% (334/344) (95% CI = 94.7%, 98.6%)	99.7% (952/955) (95% CI = 99.1%, 99.9%)
chromID™ VRE agar @48h incubation	96.9% (344/355) (95% CI = 94.5%, 98.4%)	99.7% (941/944) (95% CI = 99.1%, 99.3%)

Table 2

	Positive % Agreement	**Negative % Agreement**
BEAV agar @ 24h incubation	87.2% (300/344) (95% CI = 83.2%, 90.6%)	100.0% (955/955). (95% CI = 99.6%, 100.0%)
BEAV agar @ 48h incubation	91.8% (326/355) (95% CI = 88.5%, 94.5%)	100.0% (944/944) (95% CI = 99.6%, 100.0%)

Table 3 - Performance vs. VITEK® 2 ID: *E. faecium*

E. faecium	**Positive % Agreement**	**Negative % Agreement**
chromID™ VRE agar @ 24h incubation	94.3% (316/335) (95% CI = 91.3%, 96.6%)	11.1% (1/9)* (95% CI = 0.3%, 42.3%)
chromID™ VRE agar @ 48h incubation	96.7% (324/335) (95% CI = 94.2%, 98.4%)	0.0% (0/9)* (95% CI = 0.0%, 33.6%)

* Of the nine isolates that were not identified as *E. faecium* by VITEK 2, one isolate was negative on the chromID™ VRE at 24 hours but was false positive after 48 hours. The other eight isolates were false positive on chromID™ VRE at 24 and 48 hours.

Table 4 – Performance vs. VITEK® 2 ID: *E. faecalis*

E. faecalis	Positive % Agreement	Negative % Agreement
chromID™ VRE agar @ 24h incubation	87.1% (27/31) (95% CI = 70.2%, 96.4%)	0/0*
chromID™ VRE agar @ 48h incubation	96.8% (30/31) (95% CI = 83.3%, 99.9%)	0/0*

* All *E. faecalis* isolates were identified by VITEK 2 however four isolates did not produce the characteristic blue-to-green color at 24 hours. At 48h incubation, three of the four isolates developed the characteristic blue-to-green color.

Table 5 - Performance vs. Vancomycin MIC: *E. faecium*

E. faecium	Positive % Agreement	Negative % Agreement
chromID™ VRE agar @ 24h incubation	94.4% (321/340) (95% CI = 91.4%, 96.6%)	25.0% (1/4)* (95% CI = 0.6%, 80.6%)
chromID™ VRE agar @ 48h incubation	97.1% (330/340) (95% CI = 94.7%, 98.6%)	25.0% (1/4)* (95% CI = 0.6%, 80.6%)

* Three of four isolates were false positive as they produced violet colonies on chromID™ VRE but were confirmed to be vancomycin susceptible *E. faecium* by MIC. The fourth isolate did not produce violet pigmented colonies.

Table 6 - Performance vs. Vancomycin MIC: *E. faecalis*

E. faecalis	Positive % Agreement	Negative % Agreement
chromID™ VRE agar @ 24h incubation	86.7% (26/30) (95% CI = 69.3%, 96.3%)	0.0% (0/1)* (95% CI = 0.0%, 97.5%)
chromID™ VRE agar @ 48h incubation	96.7% (29/30) (95% CI = 82.8%, 99.9%)	0.0% (0/1)* (95% CI = 0.0%, 97.5%)

* One sample produced blue-to-green colonies on chromID™ VRE and was vancomycin susceptible by MIC.

Challenge Testing:

Seventy-five well-characterized challenge strains including vancomycin-resistant and vancomycin-susceptible *E. faecalis* and *E. faecium*, as well as Gram-positive microorganisms commonly isolated from stool, were evaluated on chromID™ VRE agar and produced the expected results. One challenge isolate, *E. faecalis* 13029 (*van*B) produced blue-purple colonies after 48 hours incubation. This was due to a rare situation of activity of both enzymes (α-glucosidase and β-galactosidase) occurring in one strain. Both enzymes reacted with the chromogen in the chromID™ VRE agar and this mixture of activity produced the blue-purple color variation.

A second study was performed to evaluate the detection of enterococcal strains with low level vancomycin resistance. Forty-nine enterococci strains characterized by intermediate or low levels of resistance to vancomycin were evaluated. *E. faecium* and *E. faecalis* with a low level of vancomycin resistance, such as those carrying the *vanB* gene are detected on chromID™ VRE medium with their characteristic colony color if their vancomycin MIC is ≥ 4 µg/mL. For a majority of isolates, the characteristic colony coloration is observed after 48 h of incubation. *E. casseliflavus* strains are inhibited on chromID™ VRE. *E. gallinarum*

strains are inhibited on chromID™ VRE unless they have an acquired *vanA gene*. In this case, characteristic violet color is observed after 48 h.

Interference Study

Commonly used medicinal substances, blood, Cary Blair Transport medium and physiological saline were evaluated for potential interference with the chromogenic reaction of the chromID™ VRE agar. None of the potentially interfering substances tested affected the performance of the chromogenic reaction of the chromID™ VRE medium but decreases in the quantity of growth were observed. Cary Blair Transport medium did not interfere with the chromogenic reaction of the chromID™ VRE agar or reduce the quantity of growth on the plate. In the presence of Preparation-H Cream or Miconazole-7, the detection of certain resistant E. faecalis or E. faecium isolates may be inhibited or delayed after 24 to 48 hours incubation on the chromID™ VRE medium. Other commonly used medicinal substances, blood and physiological saline may result in decreased growth.

Reproducibility

Ten reproducibility organisms comprised of a subset of challenge isolates representing Vancomycin susceptible and resistant *E. faecalis* and *E. faecium* (both *van*A & *van*B), as well as quality control reference strains, were evaluated by chromID™ VRE in triplicate each day for three days at each clinical trial site and produced the expected results. Preliminary results after 24 hours of incubation show 80% reproducibility for this set of organisms. After the chromID™ VRE plates were incubated for the full 48 hours, overall reproducibility was 100% for this set of organisms.

Cross Reactivity Study

A cross reactivity study was performed to determine if strains other than vancomycin-resistant enterococci could grow on chromID™ VRE agar and develop violet or blue-to-green colonies. Ninety-nine organisms were included in the cross-reactivity study. Five strains developed violet or blue-to-green pigmented colonies. These included one strain each of *Candida albicans, C. tropicalis, Citrobacter freundii, Enterococcus raffinosus* and two strains of *Klebsiella pneumoniae*. Several micro-organisms other than enterococci (including yeasts and Gram-negative bacilli), may grow and or develop pigmented colonies on chromID™ VRE. On rare occasions colonies may produce violet or blue-to-green pigment.

Recovery Study

A recovery study was performed to define the lowest number of colony forming units (CFU) of vancomycin-resistant enterococci (VRE) that could grow on the chromID™ VRE medium. One strain each of *Enterococcus faecalis (VRE)* and *E. faecium (VRE)* were evaluated. A series of 10-fold serial dilutions were prepared in saline and then plated in duplicate onto chromID™ VRE medium. After 48 hours incubation, the number of CFU was counted on each plate. The number of CFU obtained on the two plates from each dilution was averaged. The lowest number of CFU that can be detected on chromID VRE is equivalent to a theoretical 100 CFU per mL of sample.

Swab Study

The impact of swabs on the detection of *E. faecium* or *E. faecalis* (VRE) with chromID™ VRE medium was evaluated. Rayon swabs and nylon flocked swabs were tested dry and with Amies transport medium. The study evaluated detection of VRE based on contact times of 1, 4 and 18 hours for each swab type both at room temperature and at 2-8°C. The organism test set included 16 strains of *vanA* or *vanB* positive *Enterococcus faecalis* and *E. faecium* with various vancomycin MIC values. Results indicated that after 1 h and 4 h of contact, there was no significant difference in the sensitivity of detection between dry swabs and those in Amies transport medium. After 18 h of contact at room temperature, the nylon flocked swab with Amies media had the best results followed by the nylon flocked dry swab and rayon swab w/ Amies transport medium. After 18 h of contact at 2-8°C, the nylon flocked swabs with and without Amies media had the best results followed by the rayon swabs with and without Amies transport medium.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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MAR 0 2 2010

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Re: K091025
Trade/Device Name: chromID™ VRE Agar
Regulation Number: 21 CFR 866.1700
Regulation Name: Culture Media, Antimicrobial Susceptibility Test, Excluding Mueller Hinton Agar
Regulatory Class: Class II
Product Code(s): JSO
Dated: April 8, 2009
Received: April 10, 2009

Dear Ms. Weaver:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

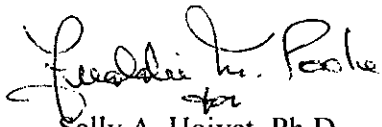
If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



Sally A. Hojvat, Ph.D.
Director, Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Indications for Use

510(k) Number (if known): K091025

Device Name: chromID™ VRE Agar

Indications For Use:

chromID™ VRE agar is a selective and differential chromogenic medium containing 8 µg/mL of vancomycin, for the qualitative detection of *Enterococcus faecium* and *E. faecalis* showing acquired vancomycin resistance (VRE) in stool specimens. chromID™ VRE agar can be used as an aid to identify, prevent and control VRE colonization in healthcare settings. chromID™ VRE agar is not intended to diagnose VRE infection nor to guide or monitor treatment for infections. Subculture to non-selective media (e.g. trypticase soy agar with 5% sheep blood) is needed for further identification, susceptibility testing and epidemiological typing.

Prescription Use X AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K091025